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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,277	11/28/2000	Oivin M. Guicherit	CIBT-P04-072	7556
28120	7590	10/21/2004	EXAMINER	
ROPE & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			RAO, DEEPAK R	
			ART UNIT	PAPER NUMBER

1624

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/724,277

**Applicant(s)**

GUICHERIT ET AL.

**Examiner**

Deepak Rao

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-45 ~~are~~ are pending in the application.
- 4a) Of the above claim(s) 41-43 ~~are~~ are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-40, 44 and 45 ~~are~~ are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>032204</u> . | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

This office action is in response to the amendment filed on July 26, 2004.

Claims 1-45 are pending in this application.

#### ***Election/Restrictions***

Claims 41-43 are withdrawn from further consideration as being drawn to non-elected inventions.

#### ***Withdrawn Rejections:***

Applicant is notified that any outstanding rejection that is not expressly maintained in this office action has been withdrawn in view of applicant's remarks.

#### ***The following rejections are maintained:***

1. Claims 1-40 and 44-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a method of inhibiting hedgehog pathway in a cell having a functional patched receptor by administering an effective amount of a compound of formula II or III, does not reasonably provide enablement for the claimed method for all other compounds and/or **means** embraced by the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is nearly connected, to use the invention commensurate in scope with these claims. The reasons provided in the previous office action are incorporated here by reference.

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Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant cites MPEP sections 2164.05(a) and 2164.04 and argues that the burden is on PTO to establish a prima facie case of lack of enablement. As indicated in the previous office action(s), the instant claims encompass the administration of any compound that "inhibits the hedgehog pathway in a cell having a functional patched receptor but does not inhibit the hedgehog pathway in a patched-null cell", however, there appears to be no disclosure such molecules, other than those of structural formula II and III in the specification, nor guidance as to how to produce such a molecule generally. The claims claim a method using such a molecule, yet the specification appears to offer no guidance other than an invitation to the skilled artisan to perform random trial and error experimentation to try to find such a molecule. For example, the specification on pages 29-30 provides that compounds of formula I are useful in the claimed method, however, the provided structural formula reads on molecules such as H<sub>2</sub>, CH<sub>4</sub>, etc. and applicant has not provided if these molecules also meet the required criteria of functional patched receptor. Therefore, due to lack of direction/guidance in the specification regarding which structural features are required for a therapeutic compound that inhibits the hedgehog pathway in the cell having a functional patched receptor, the absence of working examples other than those of quinazoline core, the complex nature of the effect of hedgehog pathway effects, the breadth of the claims which encompasses a multitude of structurally distinct compounds, and the state of the art which does not appear to sufficiently disclose compounds with the required activity, undue experimentation would be required of the skilled artisan to make and use the claimed invention.

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Contrary to what applicant urge by citing *In re Marzocchi*, 169 USPQ 367, the examiner has provided both reasoning including the nature of the invention which is directed to an unpredictable art, citation of case law as well as relevant publication to support the reason for the rejection.

Applicant relies on the 50+ examples provided in the specification for structural diversity, however, all of the compounds have a common structural core of a quinazoline or a indolopyrido group (tricyclic). There is no disclosure of structural relatedness between these compounds and other compounds that are potentially useful in the claimed method.

Applicant argues that ‘one skilled in the art would readily have been able to identify additional compounds within the scope of those recited in the claims through the use of chemical libraries’ – however, in order to prepare a chemical library, identification of the appropriate scaffold is necessary. The specification does not provide sufficient guidance of structural features or the chemical identity of the compounds useful in the claimed method. On the other hand, provides only an invitation to perform random trial and error experimentation to identify which structural backbone may potentially bear the characteristics of the compounds intended in the method.

Further, see *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003) wherein the District Court found that the claims were “reach through” claims because ‘no disclosure of inhibitor or structure or physical properties, and inhibitor structure could not be deduced from any known correlation’ and held that ‘the claimed method was not adequately described’.

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2. Claims 1-40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-35 of U.S. Patent No. 6,545,005. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims substantially overlap the reference claims. The reference also teaches a method of inhibiting hedgehog pathway with a hedgehog antagonist of formula II. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the hedgehog antagonists including those taught by the reference, because the skilled chemist would have had the reasonable expectation of obtaining similar results.

This rejection was made in the previous office action, applicant has neither argued nor addressed the rejection in the response filed on July 26, 2004. The rejection is also applied to the newly filed claims 44-45 for the reasons provided above.

***The following rejections are under new grounds:***

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-40 and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/41545. The reference teaches a method for inhibiting aberrant growth states resulting from hedgehog pathway in an amount sufficient to antagonize hedgehog activity, see pages 16-18. The instant claims differ by requiring that the compound does not inhibit the hedgehog pathway in a patched-null cell. The reference, however, teaches the use of small molecules that antagonize activity of the hedgehog pathway and the instantly recited characteristic, is inherently possessed by the reference disclosed small molecules. One of ordinary skill in the art would have been motivated use the reference disclosed small molecules in the instant method with the reasonable expectation of success in inhibiting hedgehog pathway in a cell having functional patched receptor.

Applicant relies on the Ptc-null assay disclosed in specification page 95 to distinguish the reference compounds from the compounds of the instant invention, however, there is no data provided for the reference compound and the compounds of the invention. The specification provides that 'jervine significantly decreased the expression of gli-1 mRNA in ptc-null cells as compared to the compounds of the invention which did not show significant decrease in the expression of gli-1'. There was no quantitative analysis to show that the compounds of the instant claims are in fact different and possess superior activity. In the absence of such data, it has been held that the instantly claimed method would have been obvious to one of ordinary skill in the art.

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***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation “an effective amount of means” is confusing and unclear. It is not understood what is intended by the term “means”. The specification does not provide any explanation and the amendment does not direct to any part of the specification where the term is explained.

***Duplicate Claims***

Applicant is advised that should claim 1 be found allowable, claim 44 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The term “means” in claim 44 does not distinguish sufficiently from the recitation of ‘a compound’ of claim 1.

Applicant is advised that should claim 30 be found allowable, claim 45 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other



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as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The term “means” in claim 45 does not distinguish sufficiently from the recitation of ‘a compound’ of claim 30.

### ***Specification***

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Page 21 has some structural formulae at lines 25-27 that are not legible. Appropriate amendment is required.

Receipt is acknowledged of the Information Disclosure Statement filed on March 22, 2004 and a copy is enclosed herewith.

### ***Conclusion***

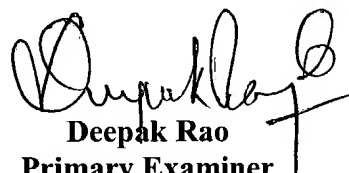
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (571) 262-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



**Deepak Rao**  
**Primary Examiner**  
**Art Unit 1624**

October 18, 2004